Contribution of Susceptibility Weighted Imaging Sequence of MRI to Diagnosis of Parkinson's Disease

Eurasian Clinical and Analytical Medicine Original Research

SWI Seqeuence in Parkinson Disease

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Abstract

Aim: Parkinson disease is the second most common neurodegenerative disease. In Parkinson disease, iron content in basal ganglia of the brain increases. In the present study the contribution of susceptibility weighted imaging (SWI) to the diagnosis of Parkinson disease was evaluated by investigating iron deposition in the basal ganglia of Parkinson disease patients.

Material and Methods: Thirty-five patients who had a clinical diagnosis of Parkinson disease and nineteen patients with a diagnosis of headache from the neurology clinic of our hospital from a similar age group were selected. Magnetic resonance images of the patients were compared retrospectively with the images obtained from the control group. Demographic data, disease duration, age of first diagnosis and Parkinson clinical scores of the patients were recorded. Intensity measurements of the basal ganglia were obtained in SWI sequence. To make a quantitative analysis signal-noise ratio (SNR) was calculated from obtained measurements.

Results: SNR results obtained from the basal ganglia with SWI sequence were significantly lower in the patient group compared with that from the control group ($p<0.05$). There was no correlation within the patient group between clinical score, disease duration, patients' age of first diagnosis and SNR results ($p>0.05$).

Discussion: SWI sequence of magnetic resonance imaging may be used as supporting method for the diagnosis of Parkinson disease but it was not found very helpful in evaluating clinical severity, side of involvement and progression of the disease.

Keywords

Iron; Magnetic Resonance Imaging; Parkinson Disease; SWI

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Introduction

Parkinson's disease (PD) is a neurodegenerative disease characterized by resting tremor, rigidity, bradykinesia, and postural instability [1]. Due to the current lack of a specific diagnostic method, PD is diagnosed clinically [2].

The basal ganglia are thought to have a tendency towards mineralization and iron accumulation due to their high metabolic activity [3]. Iron (Fe) is claimed to catalyze the over-production of reactive free radicals in mitochondria, thus causing neurodegeneration [4]. As a result, there is a need for in vivo imaging techniques that are especially sensitive to Fe accumulation.

Magnetic resonance imaging (MRI) has the highest soft tissue resolution among the radiological diagnostic methods without ionizing radiation [5] and therefore is frequently used in evaluating PD patients [6-8]. T2 relaxation time is measured for the evaluation of Fe accumulation in PD patients [2]. Fe accumulation causes the T2 relaxation time to shorten and decrease in the signal intensity of the affected tissues.

Susceptibility weighted imaging (SWI) has been developed to strengthen the contrast in the T2* sequence [9]. SWI uses the susceptibility difference among surrounding tissues to achieve tissue contrast. Also, it shows the blood products and calcium better than the other gradient echo sequences [10]. Phase images of SWI sequence give extensive information regarding the local susceptibility changes between tissues [11], thereby increasing the sensitivity in detecting local changes in Fe contents [12].

This study aimed to use SWI sequence to evaluate Fe accumulation in the basal ganglia of PD patients and examine the clinical correlation, thereby researching the contribution of SWI sequence to the diagnosis of PD.

Material and Methods

Subjects:

Thirty-five consequtive patients (15 female, 20 male) who were followed by the neurology department with the diagnosis of PD, who were responsive to levodopa and who had a cranial MRI performed at the radiology department of a university medical faculty hospital from April 2012 to March 2013 were enrolled after the study was approved by the local ethics committee (approval date: April 25, 2013/ Nr: 2013/ 394). Patient data were obtained from their medical records and MR images were obtained from the picture archiving and communication system (PACS). Patients with a known psychiatric illness, alcohol or drug abuse, or with Alzheimer's or other kinds of dementia documented in their medical records were excluded.

From the patient records we obtained their Unified Parkinson's Disease Rating Scale (UPDRS) score [13]. This scale, which consists of 4 major sections and 42 questions, is the most commonly used scale in evaluation and follow-up of PD and related diseases. Disease onset sign and symptoms, onset lateralization site, age of diagnosis, and disease duration were recorded.

A control group was constituted with 19 individuals (8 females and 11 males) who applied to the neurology department with a complaint of headache, without any sensorimotor or cognitive deficit, without any history of stroke, diabetes mellitus, or hypertension, without any family history of PD, and who had an MRI recorded in the system.

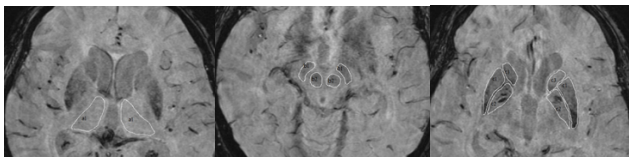

Figure 1. Drawing made on an axial plane SWI image for ROI measurements of TH (a1), SN (b1), RN (b2), PT (c1), GP (c2) and CN (c3)

MRI and Acquisition Protocol

The study images were obtained with a Hitachi Echelon 1.5 T MR system (Hitachi Medical Corporation, Tokyo, Japan), with all the cases lying in supine position and using a 16 channel head coil. Cranial MR images of the study and control groups were blindly evaluated by a radiologist who was not informed about the clinical findings.

The SWI images were obtained with the following parameters: slice thickness: 2.2 mm, echo time: 40.2 ms, repetition time: 82 ms, field of view: 220 mm, flip angle: 22°, matrix: 512x512.

Analysis of the images

These raw images were later sent to the Hitachi workstation for a manual drawing of the bilateral substantia nigra (SN), red nucleus (RN), globus pallidus (GP), caudate nucleus (CN), thalamus (TH), and putamen (PT) based on their anatomical structures. Then, region of interest (ROI) measurements were made (Figure 1). ROI of the measured basal ganglia vary based on the size of the structure.

The signal-noise ratio was calculated with the below-mentioned formula in order to perform a quantitative analysis. Background air SI was calculated from circular ROIs with an area of 0.1 cm2 of air within the coil, outside the head and free of flow-induced artifacts [14].

SNRTissue x = [mean SI Tissue x – mean SI background (air)] / standard deviation of background (air)

Statistical Analysis:

The statistical analyses were done with SPSS (Statistical Package for the Social Sciences) v.15 (Chicago, IL, USA). The normality of the data were evaluated with the Kolmogorov-Smirnov goodness of fit test. The data that fit the normal distribution were expressed as mean ± standard deviation (SD). The age difference between PD patients and healthy individuals was determined by Independent Samples t test and the similarity of gender ratio was determined by the Pearson Chi-Square test. Repeated Measures ANOVA was used to compare the right- and left-side measurements taken from the PD patients and healthy individuals. The measurements done in PD patients and the side findings were evaluated using UPDRS scores, and the correlation between the time of diagnosis of the disease and the duration of the disease was evaluated with Pearson correlation analysis. The statistical analyses were considered significant if $p < 0.05$.

Results

The patient group, which totaled 35, comprised 15 females (42.9%) and 20 males (57.1%). The mean age of the patient group was 71.17 ± 10.36 (min: 47, max: 86). In the control group, which totaled 19, there were 8 females (42.1%) and 11 males (57.9%) and the mean age was 69.78 ± 7.06 (min: 57, max: 82). There was no significant difference in the gender distribution (p=0.957) or age distribution (p=0.611) between the patient and control groups. The mean duration of disease in the PD group was 5.03 ± 4.53 (min: 1, max: 18) years and the mean age of onset was 66.14 ± 11.3 (min:35, max: 82). The mean UPDRS score of the PD group was determined as 36.89 ± 23.89 (7-109). The initial symptom was on the

Table 1. Group demographics and clinical status

	CONTROL (n 19) Mean ± SD	PARKINSON (n 35) Mean ± SD	P
Age, years	69,78±7,06	71,17±10,36	0.611
Sex (F/M)	8/11	15/20	0.912
UPDRS motor score		36,89±23,892	
Disease duration, years		5,03±4,528	
Mean onset age, years		66,14±11,3	

right side in 15 patients, the left side in 15 patients, and bilateral in 2 patients. The records regarding the unilaterality or bilaterality of the initial symptom of 3 patients were not available. These 3 patients were not included in the evaluation for side involvement (Table 1).

There was no significant side difference in the comparison of the SNR values of right and left basal ganglia in the patient and control groups (p> 0.05).

The values on both sides and the value of each basal ganglion on the same side were compared separately between the patient and control groups. Upon comparing the SNR values of the measured basal ganglia SN, RN, GP, PT, CN, and TH from the measurements obtained from the control group, the patient group's values were found to be significantly lower in all ganglia (p< 0.05) (Table 2, Figure 2).

There was no significant relationship between the SWI measurements and the UPDRS results, the duration of disease, or age of onset of disease (p> 0.05). The difference between the right- and left-side measurements of the control and the patient groups was not significant either (p> 0.05).

Discussion

Parkinson's disease (PD) is the second most common neurodegenerative disease after Alzheimer's disease and is seen in 2% of the population above the age of 60 [15]. Neurodegenerative diseases such as PD increase the iron content of the basal ganglia [3].

Table 2. Comparison of SNR values of basal ganglia of the right (R) and left (L) hemispheres of study and control groups

R	CONTROL (n 19) Mean ± SD	PARKINSON (n 35) Mean ± SD	p
PT	88,22±50,41	56,14±18,38	0.014
GP	80,76±56,02	53,64±17,42	0.053
CN	105,74±85,71	63,75±19,67	0.049
SN	91,89±64,06	54,4±17,14	0.021
RN	98,64±63,11	62,5±19,43	0.024
TH	110,18±64,29	70,97±20,33	0.018

Table 1. Group demographics and clinical status

L	CONTROL (n 19) Mean ± SD	PARKINSON (n 35) Mean ± SD	p
PT	92,36±58,53	58,36±21,24	0.024
GP	78,25±53,45	51,84±17,47	0.049
CN	104,09±68,13	66,17±20,27	0.028
SN	90,64±65,39	55,62±17,24	0.033
RN	97,05±66,04	61,89±19,99	0.035
TH	108,88±59,45	69,71±19,26	0.011

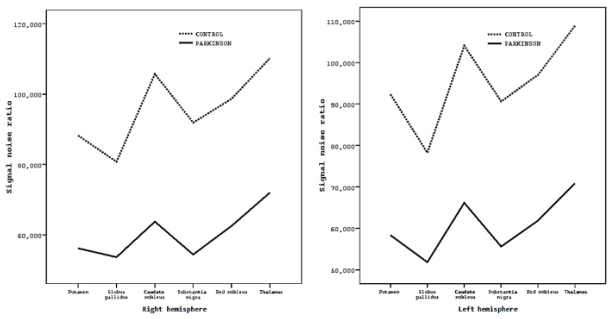

Figure 2. SNR values of basal ganglia of the right (R) and left (L) hemispheres of study and control groups

It is reported in the literature that accumulations of minerals such as iron, manganese, copper, and calcium, which are found in the post-mortem analysis of basal ganglia, are detectable with SWI–i.e., with a sequence of MRI images [3]. MRI provides the highest soft tissue resolution without ionizing radiation.

In this study, where we used the SWI sequence to evaluate the Fe distribution in the basal ganglia of PD patients, a significant decrease was detected in the SNR values of the basal ganglia of all patients with PD when compared to the measurements of the same area of the healthy individuals.

In studies where MRI was used, there are findings suggesting Fe accumulation in the basal ganglia [2,16]. In the study done by Zhang et al. using the SWI sequence on PD patients, lateralization was determined based on clinical findings and the less-affected and more-affected brain hemispheres were identified. Upon comparing the basal ganglia of the more-affected brain hemisphere with the control group, a significant relationship was found in SN only and not in the rest of the basal ganglia. On the other hand, upon comparing the basal ganglia of the less-affected side with that of the control group, no significant difference was found in any ganglia. This supports the hypothesis that there is higher iron concentration in the SN of the affected brain hemisphere of PD patients when compared with the other basal ganglia [17]. Kosta et al. did T2 relaxation time measurements in PD patients and healthy individuals. A significant decrease was detected in the pars compacta of SN (SNc) and a significant increase was detected in GPe and PT. Also, interestingly enough, they determined that the decrease of the T2 relaxation time of SNc on the affected brain hemisphere was greater than that of the less-affected brain hemisphere. Kosta et al. associated these findings with the fact that Fe concentration had increased in SNc but decreased in GPe and PT, in contrast with the literature. They claim that the Fe decrease in PT and GPe might be due to the increase in metabolic activity of these nuclei [2]. In the study of Rossi et al., which used SWI with phase masking, they contend that the SWI signals of the SN pars reticulata (SNr), RN, CN, GP, and PT are strongly suppressed and that this is due to the rich iron content [1]. The findings in our study are compatible with those of Rossi et al. The change in the accumulation of Fe in nuclei other than SNc, which are known to degenerate in PD, might be due to the rich anatomical and functional connections between these areas [2]. Our finding of significant SNR decrease in all basal ganglia aligns with this.

The literature includes studies that evaluate the relationship between UPDRS scores and the measurements in the SWI sequence [4, 16, 17]. In the SWI study of Zhang et al. in which they used phase images, they found a close correlation between the SN measurements of both hemispheres and the UPDRS scores. Due to the fact that the Fe concentration of SN is correlated with the severity of the disease, the determination of SWI phase shift values is recommended as an objective evaluation method of the severity of the disease [16]. Wallis et al. used the 'R2' = (1/T2*) – (1/T2)' formula to evaluate Fe accumulation in PD patients in order to calculate R2' relaxation ratios. In the Wallis study, a positive correlation was found between the R2' relaxation measurements of the SN of the more-affected side and the UPDRS scores, but SN did not show any correlation on the less-affected side [4]. Atasoy et al. found a negative correlation between the intensity score of the pars compacta of the SN and the UPDRS score in T2 weighted images. They could not find a correlation between the mean intensity scores of GP, RN, PT, SNr, and CN and the clinical scores [17]. We did not find any significant relationship between the SWI measurements and the UPDRS scores in our study (p> 0.05). The patient group in the present study consisted of individuals already receiving treatment, which may have caused the UPDRS scores to be lower than expected.

Studies in the literature evaluate the relationship between the measurements of the less- and more-affected brain hemispheres of PD patients [2, 4, 16]. Zhang et al. defined the brain hemisphere that is contra-lateral to the side of the body on which more symptoms of the disease, as determined by UPDRS, are considered the "more affected side" and the opposite hemisphere the "less affected side." Their study, done with SWI sequence, determined that the increase in the phase shift in only the SN of the more-affected brain hemisphere is significant as compared to the opposite side [16]. Wallis et al. found the R2' values of both sides of the patient group to be similar and Kosta et al. found the T2 relaxation times to be similar [2, 4]. In our study, we could not find a significant difference between the SWI measurements of the more-affected side and the less-affected side ($p > 0.05$).

In the literature, different results have been reported regarding the relationship between the duration and age of onset of PD and the measurements obtained in the SWI sequence [2, 4, 16, 18]. Zhang et al. and Wallis et al. could not determine a relationship between the SWI measurements and duration of disease [4,16]. Kosta et al. determined a significant decrease in the T2 relaxation time in the SN in patients who had had the disease for more than 5 years as compared to those who had had the disease for less than 5 years. They interpreted this as resulting from the increasing accumulation of iron with the increase in the duration of the disease [2]. Zhang et al. and Kosta et al. did not find any correlation between the age of onset of disease and the SWI measurements [2,16]. Bartzokis et al. made "area-dependent R2 increase" measurements and found significant increases in the SNr, SNc, PU, and GP of the patients with early-onset disease and a decrease in the "area-dependent R2 increase" in SNr of the patients with late-onset disease. They interpreted this as the difference in iron regulation between the late-onset and early-onset patients [18]. In our study, we could not find any significant relationship between the SWI measurements and the duration and age of onset of disease ($p > 0.05$). That the patients in the present study were receiving treatment may have prevented a significant Fe accumulation in the basal ganglia with increased duration of the disease.

The most important limitation of our study is that we could not use phase images due to technical problems. For this reason, we may not have been able to exclude the effects of minerals other than Fe, such as calcium, on the SWI measurements. This in turn could have caused us to fail in determining probable difference in the Fe contents of the basal ganglia. Also, in contrast to the studies that report an increase in the Fe accumulation in the basal ganglia with the progression of the disease, we believe that the reason we could not detect a relationship between the UPDRS score and the SWI measurements may be our lack of use of phase images. Our second limitation is that the individuals in the patient group were receiving treatment, which may have either slowed or prevented iron accumulation.

Conclusion

We believe that the SWI sequence may be used to support the clinical diagnosis of Parkinson's disease. This may be helpful in patients for whom the clinical picture is unclear, where an additional finding other than the clinical findings would contribute to the correct diagnosis. On the other hand, SWI sequence may not be very useful in showing the clinical severity, lateralization, or progression of the disease.

In order to demonstrate the importance of phase measurement using the SWI image, more studies with a higher number of patients who have not started medical treatment and with long term follow-ups are needed.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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